09/937,292

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NEWS 4	May 12	Polymer links for the POLYLINK command completed in REGISTRY
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NEWS 11	AUG 02	IFIPAT/IFIUDB/IFICDB reloaded with new search and display fields
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FULL ESTIMATED COST	0.21	0.21

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STRUCTURE FILE UPDATES: 30 AUG 2004 HIGHEST RN 736108-36-4
DICTIONARY FILE UPDATES: 30 AUG 2004 HIGHEST RN 736108-36-4

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http://www.cas.org/ONLINE/DBSS/registryss.html

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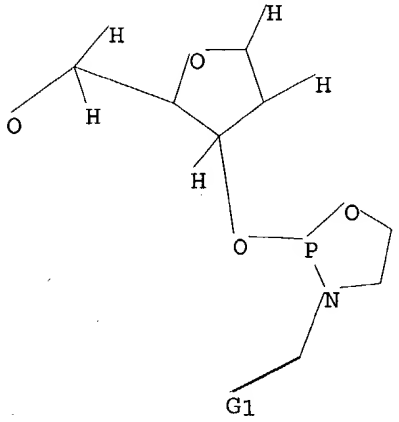

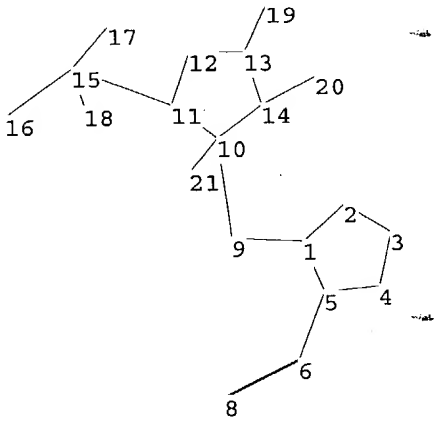

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6 8 9 15 16 17 18 19 20 21
ring nodes :
1 2 3 4 5 10 11 12 13 14
chain bonds :
1-9 5-6 6-8 9-10 10-21 11-15 13-19 14-20 15-16 15-17 15-18
ring bonds :

```
1-2  1-5  2-3  3-4  4-5  10-11  10-14  11-12  12-13  13-14
exact/norm bonds :
1-5  1-9  4-5  5-6  6-8  9-10  15-16
exact bonds :
1-2  2-3  3-4  10-11  10-14  10-21  11-12  11-15  12-13  13-14  13-19  14-20  15-17
 15-18
isolated ring systems :
containing 1 : 10 :


G1:O,S,Se

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:CLASS  8:CLASS  9:CLASS  10:Atom  11:Atom
 12:Atom  13:Atom  14:Atom  15:CLASS  16:CLASS  17:CLASS  18:CLASS  19:CLASS
20:CLASS  21:CLASS



L1      STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 16:19:06 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      0 TO ITERATE

100.0% PROCESSED       0 ITERATIONS                                0 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:            0 TO        0
PROJECTED ANSWERS:               0 TO        0

L2            0 SEA SSS SAM L1

=> s l1 ful
FULL SEARCH INITIATED 16:19:11 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -     10 TO ITERATE

100.0% PROCESSED      10 ITERATIONS                               10 ANSWERS
SEARCH TIME: 00.00.01

L3           10 SEA SSS FUL L1

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                                                       ENTRY    SESSION
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FILE COVERS 1907 - 31 Aug 2004 VOL 141 ISS 10
FILE LAST UPDATED: 30 Aug 2004 (20040830/ED)

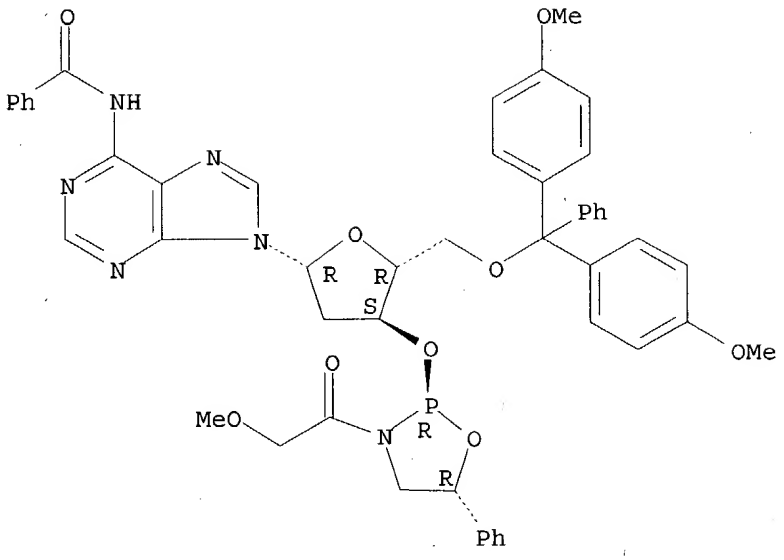
This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s l3
L4 3 L3

=> d l4 ibib hitstr abs 1-3

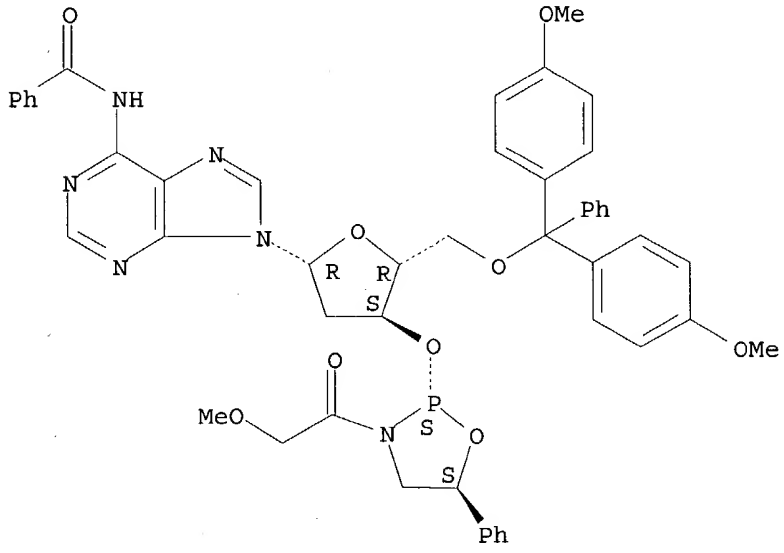
L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2002:73531 CAPLUS
DOCUMENT NUMBER: 136:232485
TITLE: Direct assignment of the absolute configuration of a distinct class of deoxyribonucleoside cyclic N-acylphosphoramidites at phosphorus by M-GOESY nuclear magnetic resonance spectroscopy
AUTHOR(S): Wilk, Andrzej; Grajkowski, Andrzej; Bull, Thomas E.; Dixon, Ann M.; Freedberg, Daron I.; Beaucage, Serge L.
CORPORATE SOURCE: Division of Therapeutic Proteins and Division of Bacterial, Parasitic & Allergenic Products, Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, MD, 20892, USA
SOURCE: Journal of the American Chemical Society (2002), 124(7), 1180-1181
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:232485
IT **403651-75-2P 403651-76-3P**
RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(direct assignment of absolute. configuration of distinct class of deoxyribonucleoside cyclic nacylphosphoramidites at phosphorus by GOESY NMR spectroscopy)
RN 403651-75-2 CAPLUS
CN Adenosine, N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-3'-O-[(2R,5R)-3-(methoxyacetyl)-5-phenyl-1,3,2-oxazaphospholidin-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 403651-76-3 CAPLUS
CN Adenosine, N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-3'-O-[(2S,5S)-3-(methoxyacetyl)-5-phenyl-1,3,2-oxazaphospholidin-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



AB The determination of the absolute configuration of deoxyribonucleoside cyclic N-acylphosphoramidites at phosphorus toward the synthesis of P-stereodifined phosphorothioated oligodeoxyribonucleotides is easily accomplished with computer-assisted mol. modeling and M-GOESY NMR spectroscopy. Specifically, computer-modeling diastereomeric phosphoramidite 3 has identified a proximal (2.55 Å) through-space interaction between benzylic H-5 and sugar H-2'', which can predictably be detected by M-GOESY NMR in SP-3 but not in RP-3 because of being too

distant (5.85 Å). Consistent with computer-assisted modeling predictions, M-GOESY NMR spectra of SP-3 and RP-3 revealed NOE signals generated from nuclei near the selectively excited H-2'' that are common to both SP-3 and RP-3, namely those of H-2', H-4', H-3', and H-1'. In addition, a diagnostic NOE signal at 5.5 ppm (benzylic H-5) is, as predicted, only detected in SP-3 and thus provides an unequivocal assessment of the configuration of the diastereomer at phosphorus. M-GOESY NMR data also confirm that the condensation of deoxyribonucleoside cyclic N-acylphosphoramidites with base-activated nucleosidic or nucleotidic 5'-hydroxyls proceeds via a single nucleophilic event.

REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2001:851807 CAPLUS
DOCUMENT NUMBER: 135:371960
TITLE: Solid phase synthesis of oligonucleotides using thermo-labile phosphorus protecting groups
INVENTOR(S): Beaucage, Serge L.; Wilk, Andrzej; Grajkowski, Andrzej
PATENT ASSIGNEE(S): The United States of America as Represented by the Department of Health and Human Services, USA
SOURCE: U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part of Appl. No. PCT/US00/04032.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2001044529	A1	20011122	US 2001-792799	20010223
US 6762298	B2	20040713		
WO 2000056749	A1	20000928	WO 2000-US4032	20000216

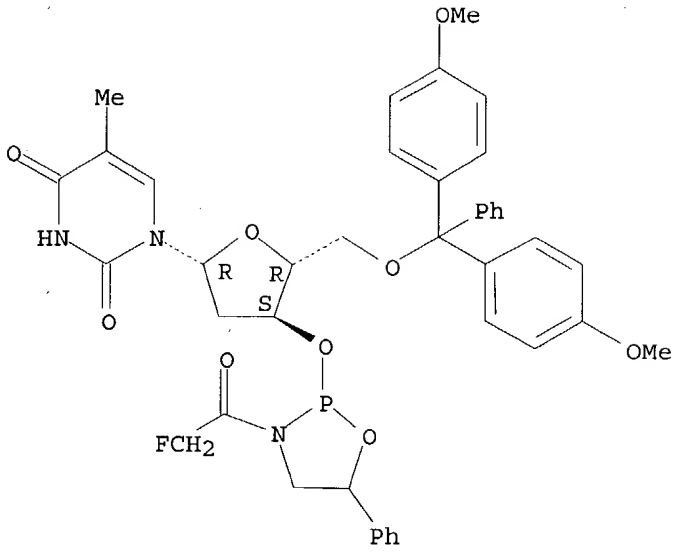
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-125867P P 19990324
WO 2000-US4032 A2 20000216

IT **373602-58-5 373602-59-6 373602-60-9**
373602-61-0
RL: RCT (Reactant); RACT (Reactant or reagent)
(solid phase synthesis of oligonucleotides using thermo-labile phosphorus protecting groups)

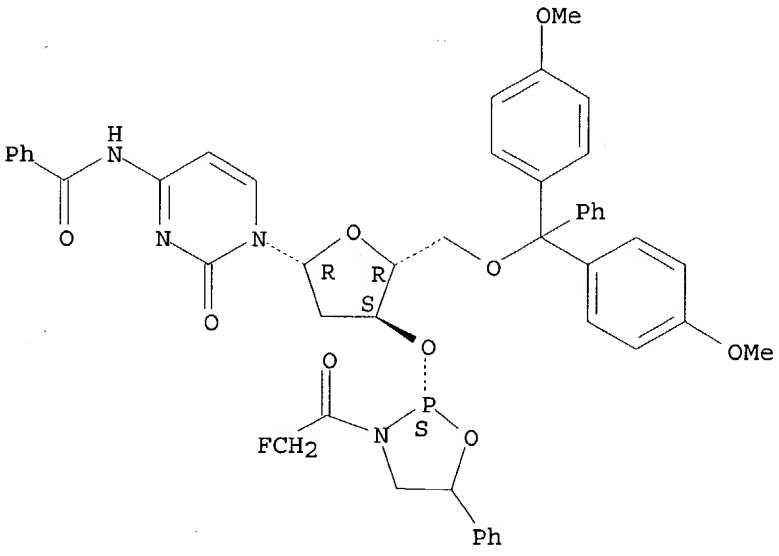
RN 373602-58-5 CAPLUS
CN Thymidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-3'-O-[3-(fluoroacetyl)-5-phenyl-1,3,2-oxazaphospholidin-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



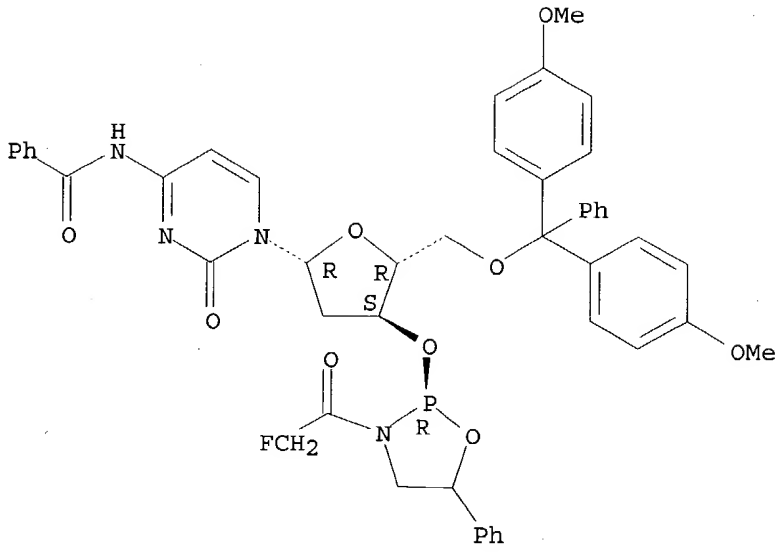
RN 373602-59-6 CAPLUS
CN Cytidine, N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-3'-O-[(2S)-3-(fluoroacetyl)-5-phenyl-1,3,2-oxazaphospholidin-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



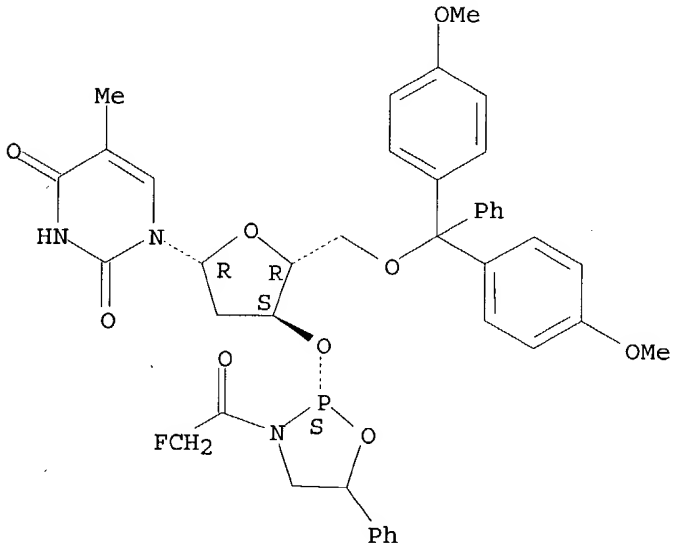
RN 373602-60-9 CAPLUS
CN Cytidine, N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-3'-O-[(2R)-3-(fluoroacetyl)-5-phenyl-1,3,2-oxazaphospholidin-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 373602-61-0 CAPLUS
CN Thymidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-3'-O-[(2S)-3-(fluoroacetyl)-5-phenyl-1,3,2-oxazaphospholidin-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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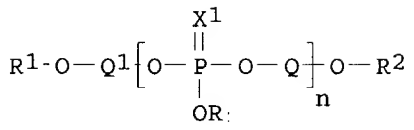

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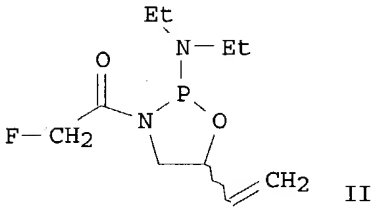


II

AB The invention provides a method of thermally de-protecting the internucleosidic phosphorus linkage of an oligonucleotide I wherein R is H or a thermolabile protecting group; R1 and R4 are independently H or hydroxyl protecting group; Q and Q1 are independently a nucleoside, oligonucleotide; X1 is O, S, Se, which method comprises heating in a fluid medium at a substantially neutral pH. The present invention further provides a method of synthesizing an oligonucleotide using the thermal deprotection method and novel oligonucleotides and intermediates that incorporate the thermo-labile protecting group used in accordance with the present invention. Thus,oxazaphospholane II was prepared and used in synthesis of oligonucleotides such as TPOT.

REFERENCE COUNT: 128 THERE ARE 128 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

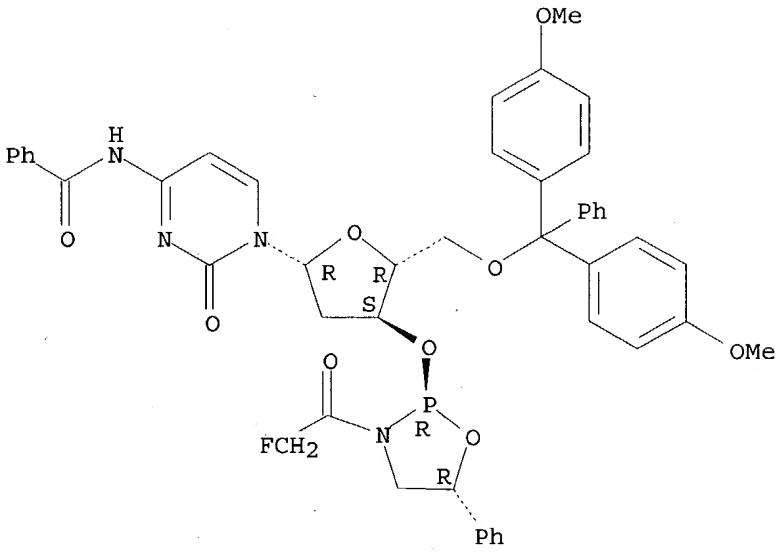
L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:125936 CAPLUS
DOCUMENT NUMBER: 132:308590
TITLE: Deoxyribonucleoside Cyclic N-Acylphosphoramidites as a New Class of Monomers for the Stereocontrolled Synthesis of Oligothymidylyl- and Oligodeoxycytidylyl-Phosphorothioates
AUTHOR(S): Wilk, Andrzej; Grajkowski, Andrzej; Phillips, Lawrence R.; Beaucage, Serge L.
CORPORATE SOURCE: Division of Therapeutic Proteins Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, MD, 20892, USA
SOURCE: Journal of the American Chemical Society (2000), 122(10), 2149-2156
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

IT **264881-16-5P 264881-45-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of deoxyribonucleoside cyclic N-acylphosphoramidites as a new class of monomers for the stereocontrolled synthesis of oligothymidylyl and oligodeoxycytidylyl phosphorothioates)

RN 264881-16-5 CAPLUS
CN Cytidine, N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-3'-O-[(2R,5R)-3-(fluoroacetyl)-5-phenyl-1,3,2-oxazaphospholidin-2-yl]- (9CI)

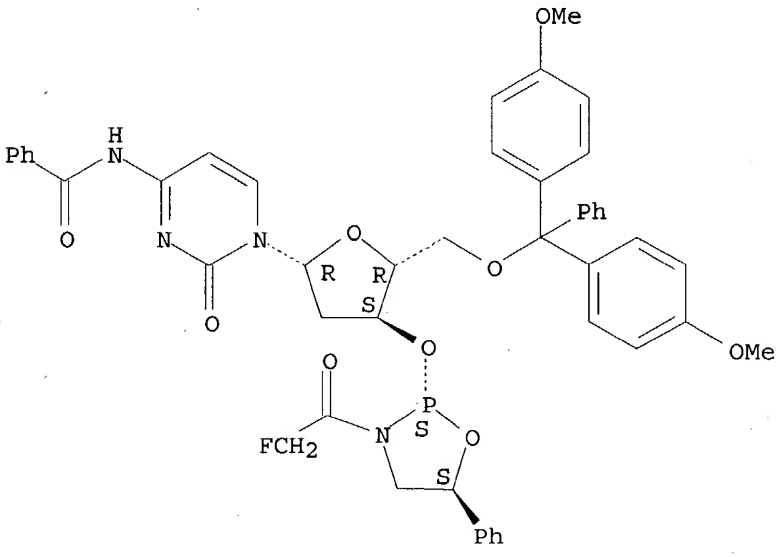
(CA INDEX NAME)

Absolute stereochemistry.



RN 264881-45-0 CAPLUS
CN Cytidine, N-benzoyl-5'-O-[bis(4-methoxyphenyl)phenylmethyl]-2'-deoxy-3'-O-[(2S,5S)-3-(fluoroacetyl)-5-phenyl-1,3,2-oxazaphospholidin-2-yl]- (9CI) (CA INDEX NAME)

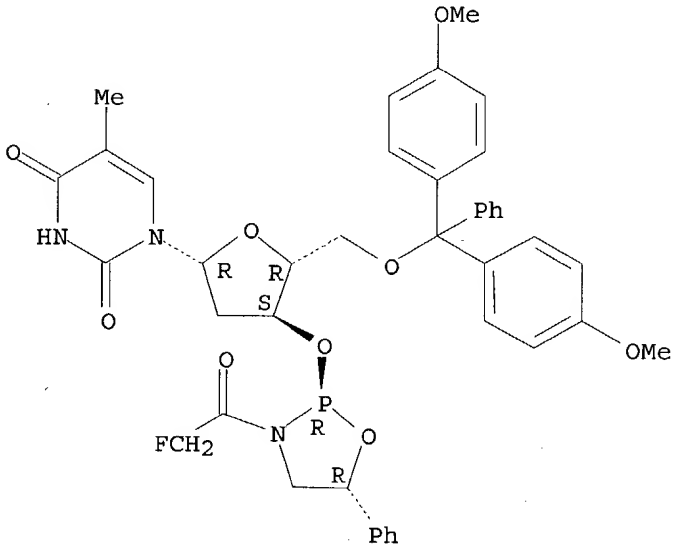
Absolute stereochemistry.



IT **264881-44-9P 264881-50-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of deoxyribonucleoside cyclic N-acylphosphoramidites as a new class of monomers for the stereocontrolled synthesis of oligothymidylyl and oligodeoxycytidylyl phosphorothioates)

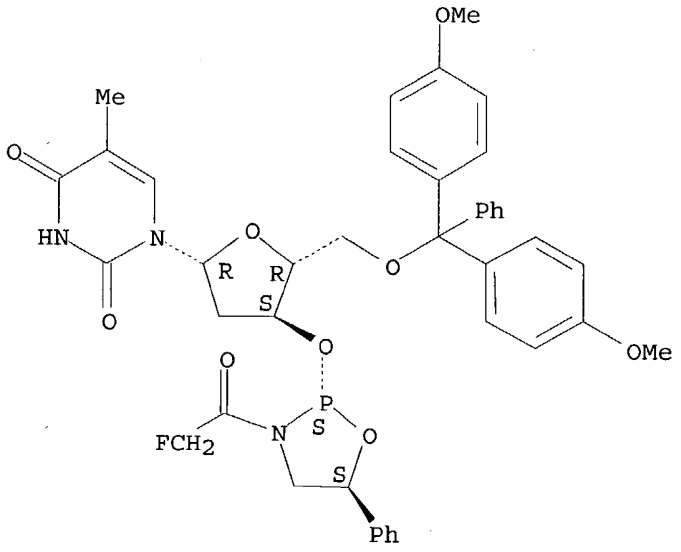
RN 264881-44-9 CAPLUS
CN Thymidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-3'-O-[(2R,5R)-3-(fluoroacetyl)-5-phenyl-1,3,2-oxazaphospholidin-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 264881-50-7 CAPLUS
CN Thymidine, 5'-O-[bis(4-methoxyphenyl)phenylmethyl]-3'-O-[(2S,5S)-3-(fluoroacetyl)-5-phenyl-1,3,2-oxazaphospholidin-2-yl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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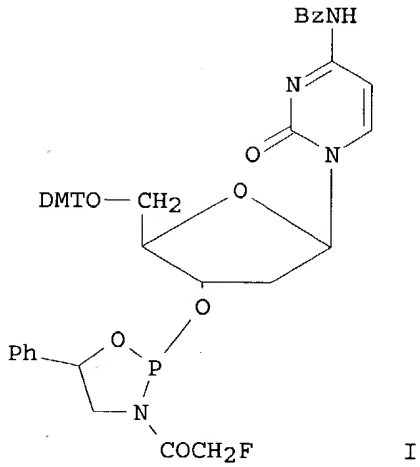

I

AB A simple and straightforward synthesis of pyrimidine 2'-deoxyribonucleoside cyclic N-acylphosphoramidites I is described. Specifically, (±)-2-amino-1-phenylethanol was chemoselectively N-acylated by treatment with Et fluoroacetate followed by reaction with hexaethylphosphorus triamide to afford the cyclic N-acylphosphoramidite as a mixture of diastereomeric rotamers. Condensation of N4-benzoyl-5'-O-(4,4'-dimethoxytrityl)-2'-deoxycytidine with the cyclic N-acylphosphoramidite in the presence of 1H-tetrazole gave, after silica gel chromatog., pure (R)- and (S)-I. 31P NMR studies indicated that when (R)- or (S)-I is reacted with 3'-O-acetylthymidine and N,N,N',N'-tetramethylguanidine in CD3CN, the dinucleoside phosphotriester is formed in near quant. yield with total P-stereospecificity (δP 144.2 or 143.9 ppm). Sulfurization generated the P-stereodefined dinucleoside phosphorothioate (δP 71.0 or 71.2 ppm). The 2'-deoxycytidine cyclic N-acylphosphoramidite derivs. (R)- and (S)-I were subsequently applied to the solid-phase synthesis of [Rp,Rp]- and [Sp,Sp]-trideoxycytidilyl diphosphorothioate d(CpsCpsC), and [Rp,Sp,Rp]-tetradeoxycytidilyl triphosphorothioate d(CpsCpsCpsC). Following deprotection, reversed-phase (RP) HPLC anal. of these oligonucleotide analogs showed a single peak for each oligomer. By comparison, RP-HPLC anal. of purified P-diastereomeric d(CpSCpSC) and d(CpSCpSCpSC) prepared from standard 2-cyanoethyl deoxyribonucleoside phosphoramidites exhibited 4 and 8 peaks, resp., each peak corresponding to a specific P-diastereomer. The thymidine cyclic N-acylphosphoramidite derivs. were also prepared, purified, and used successfully in the solid-phase synthesis of [Rp]11-d[(TpS)11T]. . Thus, the application of deoxyribonucleoside cyclic N-acyl phosphoramidites to P-stereocontrolled synthesis of oligodeoxyribonucleoside phosphorothioates may offer a compelling alternative to the methods currently used for such syntheses.

REFERENCE COUNT: 51 THERE ARE 51 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	14.72	170.35

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION

CA SUBSCRIBER PRICE -2.10 -2.10

STN INTERNATIONAL LOGOFF AT 16:19:47 ON 31 AUG 2004